Isolator Design and Air handling

ISPE – PDA Conference  Australia
Melbourne
19th September 2019

Koji Ushioda
SKAN
ushioda@skan.ch
Conventional technology v.s Isolator
Clean booth

Room: Grade B
SLR (SAL): 3
Laminar flow: Yes
Pressure control: No
Leak tight design: No
Decontamination: No
Glove access: No
Open RABS

Room: Grade B
SLR (SAL): 3
Laminar flow: Yes
Pressure control: No
Leak tight design: No
Decontamination: No
Glove access: Yes
Closed RABS

- Room: Grade B
- SLR (SAL): 3
- Laminar flow: Yes
- Pressure control: Yes
- Leak tight design: 30 to 40%/vol/h
- Decontamination: No
- Glove access: Yes
No. of recalls of sterile drugs in Australia and their source
2012 ~ 2014

<table>
<thead>
<tr>
<th></th>
<th>Risk of non sterile</th>
<th>Foreign Particles (possible risk of contamination)</th>
<th>Total no. of recalls (only Injections)</th>
<th>Ratio between sterile risk recalls and total no.</th>
</tr>
</thead>
<tbody>
<tr>
<td>2014</td>
<td>3</td>
<td>2</td>
<td>10</td>
<td>50%</td>
</tr>
<tr>
<td>2013</td>
<td>3</td>
<td>1</td>
<td>22</td>
<td>18%</td>
</tr>
<tr>
<td>2012</td>
<td>1</td>
<td>0</td>
<td>11</td>
<td>9%</td>
</tr>
<tr>
<td>US in 2014</td>
<td>3</td>
<td>2</td>
<td>NA</td>
<td>NA</td>
</tr>
</tbody>
</table>

* Data from TGA SARA

Main reason why no. of recalls based on non-sterile risk are stable is...

Conventional clean room technology!!

3 Risks of contamination caused by clean room technology
1) No pressure control
2) No decontamination
3) SLR (SAL)3
We need ultimate solution which can cover 3 Risks of contamination caused by conventional clean room technology

1) No pressure control
   => Pressure control
      Solution => SS wall and Visual through glass and glove access

2) No decontamination
   => Decontamination function to actively create aseptic environment
      Solution => H2O2 decontamination

3) SLR (SAL3)
   => SLR (SAL6)
      Solution => H2O2 decontamination and daily program

Therefore the isolator must consists of...
### Isolator

**Room:** Grade C/D  
**SLR (SAL):** 6  
**Laminar flow:** Yes  
**Pressure control:** Yes  
**Leak tight design:** Yes down to 1%  
**Decontamination:** Yes  
**Glove access:** Yes
Definition of Isolator

2. INTRODUCTION

2.1 The term ‘Isolator’ as used in the Pharmaceutical Industry covers a variety of pieces of equipment. One group has the main objective of providing containment for the handling of dangerous materials either aseptically or not. Another group has the main objective of providing a microbiologically controlled environment within which aseptic operations can be carried out.

Containment isolators often employ negative internal air pressure and most isolators used for aseptic processing employ positive pressure. A sporicidal process, usually delivered by gassing, can be used to aid microbiological control. Some large scale isolators provide an opening, often called a mousehole, to permit continuous removal of sealed product. Other isolators remain sealed throughout production operations. The capability for the isolator to be sealed allows operations to be carried out in controlled gaseous environments e.g. anaerobic conditions.

* PICs Isolators Used for Aseptic Processing and Sterility Testing
Isolator

Room: Grade C/D
SLR (SAL): 6
Laminar flow: Yes
Pressure control: Yes
Leak tight design: Yes down to 1%
Decontamination: Yes
Glove access: Yes
Major functions of isolator

- Air Tightness
- Differential pressure Control
- Filters
- AHUs
- Surrounding room
- Critical zone
- Decontamination and Daily program
- Machines
- Aseptic transfer
- Cleaning
- Qualification and Documents
- Monitoring / Alarm
- Operator Training
- Maintenance
- Sub components
Air Tightness
# Decision process of isolator leak rate

## Guideline (Internal and external)

<table>
<thead>
<tr>
<th>Pos</th>
<th>Title</th>
<th>Dokumenten ID</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Analyse der GMP Anforderungen an Isolatorsysteme</td>
<td>4-04-800-013513A04</td>
</tr>
<tr>
<td>3</td>
<td>Risikoanalyse Isolatorsysteme</td>
<td>015287_A</td>
</tr>
<tr>
<td>4</td>
<td>Risikoanalyse SIS 700</td>
<td>015293_A</td>
</tr>
<tr>
<td>5</td>
<td>Erlass der Schweizerrischen Unfallversicherungsanstalt SUVA Grenzwerte am Arbeitsplatz 2003</td>
<td>SUVA; 1903.d</td>
</tr>
<tr>
<td>6</td>
<td>Power Point Presentation H2O2 gas Concentration Measurement</td>
<td>VSL, 31.03.2004</td>
</tr>
<tr>
<td>10</td>
<td>Dichtigkeitsberechnung von Isolatoren</td>
<td>Excel Tabellen Kalkulation</td>
</tr>
</tbody>
</table>

### Outline
- Isolator Analysis (GMP)
- ISO
- Containment Leak test method
- Isolator system risk analysis
- Risk analysis SIS700
- Swiss accident insurance
- Limitation for work station
- H2O2 gas concentration measurement
- H2O2 sensor calibration method
- Distribution of H2O2 gas
- Use of H2O2 sensor
- Calculation of isolator leak
Complex Pressure Control of Fill Finish Production Isolators (aseptic and aseptic/toxic)
Pressure

Vial line (aseptic only)

Air Flow (by design, depending on phase)
Reduce potential spreading – pressure control

Fill to lyophilize loading

Air Flow (by design, depending on phase)
Air Handling goes to GREEN.
Area for AHU and Electrical Panels
Thank you